

IN THE CLAIMS

Please amend the claims as follows:

Claims 1-26 (Canceled).

Claim 27 (Currently Amended): A method of screening ~~[[the]]~~ operating conditions of a coupling reaction of at least two functional groups, comprising ~~which comprises the following steps:~~

i) reacting together at least two compounds:

[[•]] a first compound of formula  $E_1-X_1-G_1$  in which  $G_1$  represents a first of said at least two functional groups,  $X_1$  represents a covalent bond or a first spacer group, ~~while~~ and  $E_1$  represents the residue of a first molecule  $M_1$  for which a first specific antibody  $AC_1$  is available[[,]]; and

[[•]] a second compound of formula  $E_2-X_2-G_2$  in which  $G_2$  represents a second of said at least two functional groups,  $X_2$  represents a covalent bond or a second spacer group, which ~~may be~~ is optionally identical to or different from  $X_1$ , ~~while~~ and  $E_2$  represents either ~~[[the]]~~ a residue of a second molecule  $M_2$  that is different from  $M_1$  and for which a second specific antibody  $AC_2$  is available, or a group capable of forming at least one covalent bond with the antibody  $AC_1$  in the presence of a coupling agent[[;]].

wherein said at least two compounds ~~being reacted~~ are reacted in a solution comprising ~~in~~ a solvent ~~and~~ under predetermined operating conditions, ~~at least one of which is comprising a candidate operating condition, in order to obtain a reaction medium and the formation, in [[this]]~~ the reaction medium, ~~of to obtain~~ a compound Z comprising the chain  $E_1-X_1-G_1-G_2-X_2-E_2$  comprising the  $E_1$ ,  $X_1$ ,  $E_1$  and  $E_2$  ~~in which  $X_1$ ,  $X_2$ ,  $E_1$  and  $E_2$  have the same meaning as above, while, wherein~~  $G_1-G_2$  represents the group of atoms resulting from the coupling of said at least two functional groups;

ii) determining the concentration of the obtained compound Z in the reaction medium at a predetermined reaction time  $t$ , by ~~means of~~ at least one immunoassay ~~using~~ comprising at least the antibody AC<sub>1</sub>; and

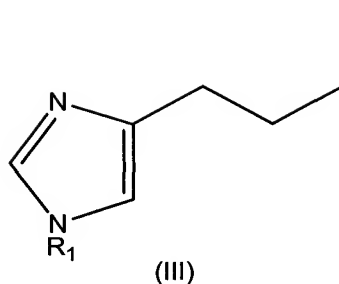
iii) evaluating the effects of the candidate operating condition(s) on said coupling reaction ~~using~~ by the concentration of compound Z thus determined.

Claim 28 (Currently Amended): The method according to Claim 27, ~~in which~~ wherein the coupling reaction is ~~chosen~~ selected from the group consisting of esterification reactions, amidation reactions, aldolization and nitroaldolization reactions, the Heck reaction, the Baylis-Hillman reaction, the Michael reaction, metathesis reactions, the Diels-Alder reaction, the Sonogashira reaction, the Suzuki reaction, the Kumada reaction, the Stille reaction, the Hiyama reaction, the Liebeskind-Srogl reaction, the Mannich reaction, the Hantzsch reaction, the reaction comprising coupling an  $\alpha$ -ketoaldehyde with a carboxylic acid and an isonitrile to obtain an oxazole ~~of Bossio et al.~~, the Ugi reaction, and variants thereof.

Claim 29 (Previously Presented): The method according to Claim 27, in which E<sub>1</sub> or E<sub>2</sub> represents the histamine residue.

Claim 30 (Canceled).

Claim 31 (Currently Amended): The method according to Claim 29, in which E<sub>1</sub> or E<sub>2</sub> ~~corresponds to~~ is a compound of formula (III) below:



in which R<sub>1</sub> represents a hydrogen atom or a protective group.

Claim 32 (Canceled).

Claim 33 (Previously Presented): The method according to Claim 27, in which E<sub>2</sub> represents a group chosen from amine, carboxylic acid, aldehyde, thiol, phenol, alkenyl and azide groups, and photoactivatable groups.

Claim 34 (Previously Presented): The method according to Claim 33, in which E<sub>2</sub> represents an amine or thiol group.

Claim 35 (Previously Presented): The method according to Claim 27, in which said at least one immunoassay for the compound Z is a solid-phase assay.

Claim 36 (Canceled).

Claim 37 (Currently Amended): The method according to Claim 27, wherein ~~in which, since E<sub>2</sub> corresponds to~~ is a group capable of forming at least one covalent bond with the first antibody AC<sub>1</sub>, ~~step and the ii) comprises the following steps:~~

a<sub>2</sub>) bringing the reaction medium obtained at reaction time  $t$  into contact with a solid phase on which the first antibody  $AC_1$  is immobilized, so as to obtain the attachment of the compound Z to ~~this~~ the solid phase by immunobinding between ~~[[this]]~~ the antibody  $AC_1$  and the residue  $E_1$  of ~~[[this]]~~ the compound  $Z$ ;

b<sub>2</sub>) reacting a coupling agent with the first antibody  $AC_1$  immobilized on the solid phase and the group  $E_2$  of the compound Z attached to ~~[[this]]~~ the solid phase, so as to obtain the formation of one or more covalent bonds between ~~[[this]]~~ the antibody  $AC_1$  and ~~[[this]]~~ the group  $E_2$ ;

c<sub>2</sub>) denaturing the immunobond which exists between the first antibody  $AC_1$  immobilized on the solid phase and the residue  $E_2$  of the compound Z attached to ~~[[this]]~~ the solid phase, so as to release ~~[[this]]~~ the residue  $E_2$  from ~~[[this]]~~ the solid phase;

d<sub>2</sub>) bringing the solid phase into contact with a conjugate comprising the first antibody  $AC_1$  coupled to a label, so as to obtain the attachment of ~~[[this]]~~ the conjugate to ~~[[this]]~~ the solid phase by immunobinding between ~~[[said]]~~ the antibody  $AC_1$  and the residue  $E_1$  of the compound  $E_1-X-G_1-G_2-Y-E_2$  thus released;

e<sub>2</sub>) measuring the amount of conjugate attached to the solid phase by ~~means of~~ the label coupled to the antibody  $AC_1$ ; and

f<sub>2</sub>) determining, on a standard range, the concentration of compound Z in the reaction medium at said time  $t$ , from the amount of conjugate thus measured;

said ~~[[step]]~~ ii) ~~[[also]]~~ further comprising one or more operations comprising ~~consisting in~~ washing the solid phase, between ~~[[steps]]~~ a<sub>2</sub>) and b<sub>2</sub>), b<sub>2</sub>) and c<sub>2</sub>), c<sub>2</sub>) and d<sub>2</sub>), and between ~~[[steps]]~~ d<sub>2</sub>) and e<sub>2</sub>).

Claim 38 (Previously Presented): The method according to Claim 27, in which the first antibody  $AC_1$  is a monoclonal antibody.

Claim 39 (Canceled).

Claim 40 (Previously Presented): The method according to Claim 27, in which the solid phase is the wall of a well of a microtitration plate onto which the first antibody AC<sub>1</sub> is adsorbed.

Claim 41 (Canceled).

Claim 42 (Currently Amended): The method according to Claim 27, which comprises an operation comprising ~~consisting of~~ dilution of the reaction medium between the [[steps]] i) and ii).

Claim 43 (Previously Presented): The method according to Claim 27, in which the yield of the coupling reaction is determined from the concentration of compound Z in the reaction medium.

Claim 44 (Currently Amended): The method according to Claim 27, in which the coupling reaction ~~consists in~~ comprises coupling 2, 3 or 4 functional groups.

Claim 45 (Currently Amended): The method according to Claim 44, in which the coupling reaction ~~consists in~~ comprises coupling two functional groups G<sub>1</sub> and G<sub>2</sub>, and in which:

——— ~~in step i)~~, the compounds of formulae E<sub>1</sub>-X<sub>1</sub>-G<sub>1</sub> and E<sub>2</sub>-X<sub>2</sub>-G<sub>2</sub> are reacted together so as to obtain ~~the formation~~, in the reaction medium, of a compound Z of which

~~corresponds to the formula  $E_1-X_1-G_1-G_2-X_2-E_2$  in which  $X_1$ ,  $X_2$ ,  $E_1$  and  $E_2$  have the same meaning as above and wherein the  $G_1-G_2$  represents the group of atoms resulting from the coupling between said functional groups  $G_1$  and  $G_2$ ; while and~~

~~——— in step ii), the concentration of compound Z in the reaction medium is determined by means of a single one immunoassay.~~

Claim 46 (Canceled).

Claim 47 (Canceled).

Claim 48 (Currently Amended): The method according to Claim 27, in which the candidate operating condition(s) is(are) ~~chosen~~ selected from the group consisting of solvents, catalysts, temperature levels, pressure levels, the use of ultrasound, concentrations, stoichiometric ratios, reaction times and combinations thereof.

Claim 49 (Previously Presented): The method according to Claim 27, in which the candidate operating condition(s) is(are) catalysts.

Claim 50 (Currently Amended): A kit for carrying out a method of screening the operating conditions of a coupling reaction of at least two functional groups, comprising ~~which comprises~~ suitable amounts:

[[ - ]] of at least two compounds reacting ~~intended to react~~ together, comprising:

[[•]] a first compound of formula  $E_1-X_1-G_1$  in which  $G_1$  represents a first of said at least two functional groups,  $X_1$  represents a covalent bond or a first spacer group and  $E_1$  represents the residue of a first molecule  $M_1$ ; and

[[•]] a second compound of formula  $E_2-X_2-G_2$  in which  $G_2$  represents a second of said at least two functional groups,  $X_2$  represents a covalent bond or a second spacer group, which ~~may be~~ is optionally identical to or different from  $X_1$ , and  $E_2$  represents the residue of a second molecule  $M_2$  which is different from  $M_1$ ;

[[ - ]] of at least two antibodies comprising:

[[•]] a first antibody  $AC_1$  specific for the first molecule  $M_1$ , ~~[[this]]~~the antibody  $AC_1$  being optionally attached to a plurality of solid phases; and

[[•]] a second antibody  $AC_2$  specific for the second molecule  $M_2$ , ~~[[this]]~~the antibody  $AC_2$  being coupled to a label;

[[ - ]] of a compound Z comprising the chain  $E_1-X_1-G_1-G_2-X_2-E_2$  ~~in which  $X_1$ ,  $X_2$ ,  $E_1$  and  $E_2$  have the same meaning as above, while~~ , wherein the  $G_1-G_2$  represents the group of atoms resulting from the coupling of said at least two functional groups; and, optionally:

[[ - ]] of a reagent for visualizing the label, ~~for example a substrate if the label is an enzyme~~; and

[[ - ]] of suitably chosen buffers.

Claim 51 (Currently Amended): A kit for carrying out a method of screening the operating conditions of a coupling reaction of at least two functional groups, comprising ~~which comprises~~ suitable amounts:

[[ - ]] of at least two compounds reacting ~~intended to react~~ together comprising:

[[•]] a first compound of formula  $E_1-X_1-G_1$  in which  $G_1$  represents a first of said at least two functional groups,  $X_1$  represents a covalent bond or a first spacer group and  $E_1$  represents the residue of a first molecule  $M_1$ ; and

[[•]] a second compound of formula  $E_2-X_2-G_2$  in which  $G_2$  represents a second of said at least two functional groups,  $X_2$  represents a covalent bond or a second spacer group, that may be identical to or different from  $X_1$ , and  $E_2$  represents a group capable of forming one or more covalent bonds with an antibody specific for the molecule  $M_1$  in the presence of a coupling agent;

[[ - ]] of at least one antibody, this antibody being said antibody specific for the molecule  $M_1$ ;

[[ - ]] of a conjugate comprising said antibody specific for the molecule  $M_1$  coupled to a label;

[[ - ]] of a compound Z comprising the chain  $E_1-X_1-G_1-G_2-X_2-E_2$  ~~in which  $X_1$ ,  $X_2$ ,  $E_1$  and  $E_2$  have the same meaning as above, while, wherein~~  $G_1-G_2$  represents [[the]] a group of atoms resulting from the coupling of said at least two functional groups; and [[,]] optionally [[:]

[[ - ]] of at least one of a reagent for visualizing the label, a coupling agent, a reagent capable of denaturing an immunobond, and suitably chosen buffers.

~~\_\_\_\_\_ of a coupling agent,~~

~~\_\_\_\_\_ of a reagent capable of denaturing an immunobond, and~~

~~\_\_\_\_\_ of suitably chosen buffers.~~

Claim 52 (Currently Amended): A method for the screening of catalysts ~~that are~~ useful in a coupling reaction between two functional groups, comprising ~~utilizing~~ the screening method according to Claim 27.



Claim 53 (Canceled).

Claim 54 (New): The method according to Claim 27, comprising:

i) reacting together at least two compounds:

a first compound of formula  $E_1-X_1-G_1$  in which  $G_1$  represents a first of said at least two functional groups,  $X_1$  represents a covalent bond or a first spacer group, and  $E_1$  represents the residue of a first molecule  $M_1$  for which a first specific antibody  $AC_1$  is available; and

a second compound of formula  $E_2-X_2-G_2$  in which  $G_2$  represents a second of said at least two functional groups,  $X_2$  represents a covalent bond or a second spacer group, which is optionally identical to or different from  $X_1$ , and  $E_2$  represents either a residue of a second molecule  $M_2$  that is different from  $M_1$  and for which a second specific antibody  $AC_2$  is available, or a group capable of forming at least one covalent bond with the antibody  $AC_1$  in the presence of a coupling agent,

wherein said at least two compounds are reacted in a solution comprising a solvent and under predetermined operating conditions comprising a candidate operating condition to obtain a reaction medium and in the reaction medium, to obtain a compound Z comprising the chain  $E_1-X_1-G_1-G_2-X_2-E_2$  comprising the  $E_1$ ,  $X_1$ ,  $E_1$  and  $E_2$ , wherein  $G_1-G_2$  represents the group of atoms resulting from the coupling of said at least two functional groups and the compound Z is attached to a conjugate attached to a solid phase;

ii) determining the concentration of the obtained compound Z in the reaction medium at a predetermined reaction time t, by at least one immunoassay comprising at least the antibody  $AC_1$ ; and

iii) evaluating the effects of the candidate operating condition(s) on said coupling reaction by the concentration of compound Z thus determined.